

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jorg Stürzebecher et al. Confirmation No.: 1588
Serial No.: 10/506,579 Art Unit: 1621
Filed: April 13, 2005 Examiner: P. Zucker
Customer No.: 21559
Title: UROKINASE INHIBITORS, PRODUCTION AND USE THEREOF

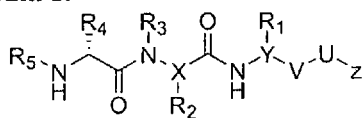
Commissioner for Patents
P.O. Box 1450
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DECLARATION OF ANDREA SCHWEINITZ UNDER 37 C.F.R. § 1.132
TRAVERSING GROUNDS OF REJECTION

Under 37 C.F.R. § 1.132 and regarding the rejection of claims 21 and 34-38 in view of Levy et al., WO 02/14349 ("Levy"), I declare:

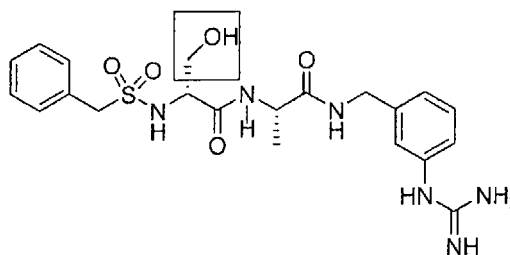
1. I am an inventor of the subject matter that is described and claimed in the above-captioned patent application.
2. As recited in currently amended claim 21, at least one of R₁, R₂, R₃ or R₅ includes one or more radicals, selected from -COOH, -CH(COOH)₂, -SO₂H, NH₂, an amidino, hydroxyamidino, amidrazono, or guanidino group, or a salt of any of these groups. The Office has cited the compound described in Example 45 of Levy, benzylsulfonyl-D-serine-L-alanine-3-guanidinobenzylamide ("the Levy compound"). As shown in the following table, the Levy -CH₂OH corresponds to R₄ in formula I and the Levy compound does not include any groups that satisfy the claimed structural requirements for any of R₁, R₂, R₃, or R₅ in instant formula I.

Corresponding Groups in Instant Formula I:



$R_1 = H$;
 $R_2 = CH_3$;
 $R_3 = H$;
 $R_4 = -(CH_2)_f OR_{11}$, where $f=1$ and R_{11} is H ;
 $R_5 = -SO_2R_{12}$, where $R_{12} =$ unsubstituted aralkyl;
 $U = \text{phenyl}$;
 $V = (CH_2)_n$, where $n = 0$;
 $X = CH$;
 $Y = (CH)_m$, where $m = 1$; and
 $Z =$ occurs in the 3-position and is a guanidino group

The Levy Compound:



In this structure, R_1 and R_3 are each H , R_2 is CH_3 , and R_5 is SO_2CH_2Ph , and none of these groups includes a radical selected from $-COOH$, $-CH(COOH)_2$, $-SO_2H$, NH_2 , an amidino, hydroxyamidino, amidrazono, or guanidino group, or a salt thereof. The Levy compound is therefore not encompassed by the claimed chemical genus.

3. Further, the 1:1 CH_2Cl_2/CF_3CO_2H solution described in Levy Example 45 would not be sufficient to protonate the serine $-CH_2OH$ group. The pK_a of a protonated serine $-OH$ group is approximately -2.85 and the pK_a of CF_3CO_2H is approximately -0.2. Based on these pK_a differences, a chemist would not expect the serine $-OH$ group of the Levy compound to be protonated in the CH_2Cl_2/CF_3CO_2H solution ($pH \sim 1-2$), in the isolated compound obtained according to the procedure described in Levy Example 45, or in the stomach ($pH \sim 1-1.5$). Consequently, a chemist would recognize that the Levy $-CH_2OH$ group is neutral under these conditions and that none of the R_1 , R_2 , R_3 , or R_5 groups in the Levy compound includes the structural features recited in the instant claims.

4. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

26.03.2010

Date

A. Schweinitz

Dr. Andrea Schweinitz